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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/831,272	08/13/2001	Christoph Kirsch	4038.001	3234

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EXAMINER	
MARVICH, MARIA	
ART UNIT	PAPER NUMBER
1633	

MAIL DATE	DELIVERY MODE
12/06/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/831,272	KIRSCH ET AL.	
	Examiner	Art Unit	
	MARIA B. MARVICH	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *9/28/10*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2,3,8,9,22,39,42-47 and 49-58* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *2, 3, 22, 42, 43, 47, 49-51* is/are allowed.

6)☒ Claim(s) *9,39,44-46,52 and 56-58* is/are rejected.

7)☒ Claim(s) *8 and 53-55* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *06 May 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This office action is in response to an amendment filed 9/28/10. Claims 2, 3, 8, 9, 22, 39, 42-47, 49-56 and 58 are pending and under examination.

Applicants' arguments are persuasive with regards to the rejection under 35 USC 112, first paragraph.

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 9, 39, 44-46, 52 and 56-58 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a new rejection necessitated by applicants' amendment.**

The limitation that the cis -element is different than a CAAT element has been added to claim 52. Applicant has not indicated where support for this limitation is found. The examiner has been unable to find support in the originally filed specification for the term "cannot be CAAT". Therefore, the limitation of adding "the cis -element is different than a CAAT element" is impermissible NEW MATTER.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 9, 39, 44-46, 52 and 56-58 are rejected under 35 U.S.C. 102(b) as being anticipated by van de Locht et al (EMBO J, 1990, vol 9(9) p 2945-2950; see entire document). **This rejection is maintained for reasons of record in the office action mailed 6/28/10. As regards claim 52, the rejection is new necessitated by applicants' amendment.**

Van de Locht et al teach a promoter obtainable by insertion of pPR2-10, which comprises at least one cis-acting element sufficient to direct elicitor-specific expression into the promoter of the GUS reporter gene as recited in claim 39. pPR2-10 comprises SEQ ID NO:I 1 as indicated in figure 5 which demonstrates that pPR2-10 comprises the region from -168 to -43. This region comprises SEQ ID NO: 11 and functions as a cis-element sufficient to direct elicitor specific expression with the CAAT element. Hence the vector comprises at least two-cis acting elements wherein the sequences of SEQ ID NO:11 and CAAT are separated by at least 50 bases. As regards elements that are different than CAAT, Van De Locht et al teach a polyA sequence. Given the broad and undefined nature of a cis element and using the guidance available in the specification, the polyA sequence which is a regulatory element that affects expression in cis meets the requirements of the claim. There are numerous other elements present in the vector such as an ATG that would also meet the requirements.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 9, 39, 44-46, 52 and 56-58 are rejected under 35 U.S.C. 103(a) as being unpatentable over Van de Locht et al (EMBO J, 1990, vol 9(9) p 2945-2950; see entire document) in view of Pears and Williams (Nucleic Acids Research, 1988, Vol 16(17), pages 8467-84861; see entire document) and Searle et al, MCB, 1985, Vol 5(6), pages 1480-1489; see entire document) further in view of Comai et al (Plant Molecular Biology, 1990, Vol 15(3), pages 373-381; see entire document). **This rejection is maintained for reasons of record in the office action mailed 6/28/10. As regards claim 52, the rejection is new necessitated by applicants' amendment.**

Applicants claim a chimeric promoter comprising at least two elements sufficient to induce pathogen mediated expression wherein at least one is SEQ ID NO: 11.

Van de Locht et al teach a promoter obtainable by insertion of pPR2-10, which comprises at least one cis-acting element sufficient to direct elicitor-specific expression into the promoter of the GUS reporter gene. pPR2-10 comprises SEQ ID NO:11 (nucleotides –77 to –46) as indicated in figure 5, which demonstrates that pPR2-10 comprises the region from -168 to -43. This region comprises SEQ ID NO: 11 and functions as a cis-element sufficient to direct elicitor specific

expression with the CAAT element. As regards elements that are different than CAAT, Van De Locht et al teach a polyA sequence. Given the broad and undefined nature of a cis element and using the guidance available in the specification, the polyA sequence which is a regulatory element that affects expression in cis meets the requirements of the claim. There are numerous other elements present in the vector such as an ATG that would also meet the requirements of a second cis element. The promoter of van de Locht et al as disclosed in Figure 5 and 6 is a chimeric promoter formed by fusion of parsley chalcone synthase promoter (which provides the minimal promoter) to a pPR2 fragment. Van de Locht et al do not teach that pPR2-10 comprises two copies of the elicitor element.

Pears and Williams teach that heterologous promoter sequences inserted into promoters can mediate sufficient gene expression (see e.g. abstract). Specifically, Pears and Williams teach that the promoter elements function "optimally" when multiple copies of the sequences are present (see e.g. page 8480 and figure 7).

Searle et al teach that promoters comprising two heterologous inducible elements isolated from the methallothionein I gene function as strong inducible promoter, whereas a single element did not respond to zinc (see e.g. abstract). Applicants reason that more than two should further increase the inducibility of the promoter.

Comai et al teach that promoters can be duplicated with the effect of enhanced expression (see e.g. abstract).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to duplicate the isolated promoter fragment that is elicitor responsive as taught by van de Locht et al as taught by Pears and Williams and Searle et al and Comai et al because and van

de Locht et al teach that a fragment of the PR2 promoter is responsible for strong elicitor mediated gene activation and because Pears and Williams and Searle et al teach that multiple elements are more effective than single elements and Comai et al teach that it is within the ordinary skill of the art to generate chimeric vectors in which larger promoter elements are duplicated. One would have been motivated to do so in order to receive the expected benefit of enhanced regulation of heterologous genes. Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Response to Argument

Applicants traverse the claim rejections in the amendment filed 9/28/10. Applicants' arguments have been fully considered but they are not persuasive. Applicants argue that Van De Locht et al does not teach that the promoter is produced by inserting at least one cis element into a gene in order to drive expression of that native gene. First, Van De Locht teaches on pages 2946 (second column) that the PR2 promoter elements are inserted into pUC9 GUS which comprises the GUS genes. While this is not a native gene, there is no explicit requirement that the gene be native. Secondly, and more to the point, the claims are drawn to a chimeric promoter. The product by process claims are not limited by their manipulation but to the structure implied by the steps (see MPEP 2113). In this case, the claims are drawn to a chimeric promoter that comprises at least one cis-acting element that comprises two or more cis elements wherein one of the elements is SEQ ID NO:11. This cis element was produced by deletion of starting fragments pPR2-01. From this a region between -168 and -43 was isolated and used to

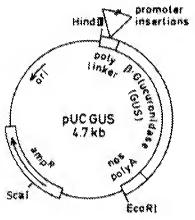
produce a PR2-CHS fusion. This fusion comprises a minimal promoter (TATA element) as well as SEQ ID NO:11 and a CAAT element. Each of these elements meet the requirements of the chimeric promoter as disclosed. It is described on page 6 that a chimeric promoter of the invention comprises for example SEQ ID NO:11 is operably linked to a minimal promoter such as from CHS. As well, the promoter comprises additional regulatory elements (cis elements) which as described by the specification on pages 6 and 9 are described quite broadly. Based upon the breadth of these acceptable definitions one would not exclude a CAAT element (see in addition to the CAAT element, the poly A signal in the figure below). The gene can be a scorable gene which GUS is.

> (page 6) It is also immediately evident to the person skilled in the art that further regulatory elements may be added to the chimeric sequences of the invention. **For example, transcriptional enhancers and/or sequences which allow for further induced expression of the chimeric promoter of the invention may be employed. Enhancer sequences functional in plants include, for example**, ocs-element (Ellis, EMBO J. 6 (1987), 3203-3208); the family of ACGT- elements (hex-motif, G-box as 1-element) (Williams, Plant Cell 4 (1992), 485-496) and the cyt-1 element (Neuteboom, Plant J. 4 (1993), 525-534).
>
> In a preferred embodiment of the chimeric promoter of the invention **the minimal promoter is derived from** the CaMV35S promoter, **CHS promoter**, PR1 promoter, or hcbt2 promoter. However, other minimal promoters from other sources may be employed as well.

> (page 8-9) Regulatory elements ensuring expression in eukaryotic, i.e. plant cells are well known to those skilled in the art. In the case of eukaryotic cells t**hey comprise optionally poly-A signals ensuring termination of transcription and stabilization of the transcript**, for example, those of the 35S RNA from Cauliflower Mosaic Virus (CaMV) and the Nopaline Synthase gene from Agrobacterium tumefaciens. **Additional regulatory elements may include transcriptional as well as translational enhancer**s. A plant translational enhancer often used is the CAMV omega sequences, the inclusion of an intron (Intron-1 from the Shrunken gene of maize, for example) has been shown to increase expression levels by up to l O0-fold. (Mait, Transgenic Research 6 (1997), 143-156; Ni, Plant Journal 7 (1995), 661-676). In this respect, it should be noted that in one embodiment of the recombinant gene of the invention **at least one of said cis-acting elements is located in the 5'- or 3-untranslated region or in an intron of the recombinant gene**
>
> **The recombinant gene of the invention can be used alone or as part of a vector to express heterologous DNA sequences, which, e.g., encode proteins** for, e.g., the control of disease resistance or diagnostics of pathogen inducible or related gene expression. The recombinant gene or vector containing the DNA sequence encoding an RNA or a protein of

interest is introduced into the cells which in turn produce the RNA or protein of interest. For example, the chimeric promoter of the invention can be operatively linked to DNA sequences encoding Barnase for use in the production of localized cell death in plants upon pathogen attack.

On the other hand, said protein can be **a scorable marker**, e.g., luciferase, green fluorescent protein or 13-galactosidase



Applicants argue that the promoter pPR2-10 is not a chimeric promoter nor a minimal promoter. However, pPR2-CHS based upon pPR2-10 is a chimeric promoter. As well, as set forth above it does comprise a minimal promoter that is fully encompassed by the instant claims (see bolded passage from page 6). Finally, applicants refer to arguments provided in the Declaration filed 3/12/07. These are ultimately that one would conclude from Van De Locht that the essential element is between -168 and -108 given the loss of expression between PR12 and PR13. However, the experimental model of Van De Locht does not support such a conclusion as Van De Locht continues experimentation with the entirety of the fragment pPR2-10. Hence, it is clear that Van de Locht recognizes that the entire fragment is critical. In fact, one could argue that the whole region comprises more than one cis -element. In other words, it is clear from Van De Locht's results that more then one element responsible for elicitor induced expression is

present in PR2. Specifically, looking at the loss of expression between PR12 and PR13 it is clear that deletion at -52 abrogates activation from this second element. That Van De That Van De Locht recognizes a critical factor in the element does not limit the teachings of Van De Locht to this single element in light of the facts that he uses the entire fragment.

Regarding the rejection under 35 USC 103, applicants point out arguments from the Declaration filed 3/12/07. Somssich argues in the Declaration filed 3/12/07 that Searle et al and Comai et al teach that duplication of promoter elements consistently leads to increased but one cannot use these findings to generalize these findings. As an initial point, KSR forecloses the argument that a specific teaching, suggestion or motivation is required to support a finding of obviousness. What is required is a teaching in the art that the means and technologies to duplicate promoter sequences are well known in the art. In this case, all of Pears, Searle et al and Comai et al teach that it was well known in the art to do so. Specifically, the teachings of Pears and Williams, Searle et al and Comai et al teach that duplication of regulatory or promoter regions is of ordinary skill in the art. Furthermore, the references teach that it is of ordinary methodology to identify those promoters that once duplicated give desired results. Specifically, Searle et al teach that promoters comprising duplication of MREs were inducible and position to one another as well as other elements had little effect (see figure 4). Comai et al teach, "There have been several reports on me effect of duplicating the 35S enhancer. In transgenic tobacco plants Kay et al. observed ten- fold enhancement in transcription by duplicating the -343 to -90 region, while Fang et al observed two-fold enhancement of transcription by duplicating the -209 to -46 region. Using transient CAT assays Odell et al. [23] did not observe any effect of duplicating the -392 to -55." While it is applicants' arguments that the failures argue against the

successes, the art teaches that there is every reason to consider duplication of regulatory regions for enhanced expression. Furthermore, the claims do not espouse any desired phenotype of the construct. Rather, claim 51 is simply drawn to duplication of a regulatory region which in this case is SEQ ID NO:11. It would have been obvious to duplicate effective regulatory regions as identified in Van De Locht given that the art teaches that duplication can lead to enhanced activity.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MARIA B. MARVICH whose telephone number is (571)272-0774. The examiner can normally be reached on M-F (7:00-4:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach, PhD can be reached on (571)-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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